RE: Consider model model simplification

Brattin, Bill to: Benson.Bob   01/14/2011 03:03 PM

From: "Brattin, Bill" <brattin@srcinc.com>
   To:

I will give it a try
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From: Benson.Bob@epamail.epa.gov [Benson.Bob@epamail.epa.gov]
Sent: Friday, January 14, 2011 4:58 PM
To: Brattin, Bill; Berry.David@epamail.epa.gov
Subject: Fw: Consider model model simplification
This seems like a good suggestion to me.
----- Forwarded by Bob Benson/R8/USEPA/US on 01/14/2011 02:57 PM -----
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From: Paul White/DC/USEPA/US
To: Bob Benson/R8/USEPA/US@EPA
Cc: Leonid Kopylev/DC/USEPA/US@EPA, Krista
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Bateson/DC/USEPA/US@EPA
        Date: 01/14/2011 02:48 PM
        Subject: Consider model model simplification

Bob,
I would like to suggest one variant on your modeling that you may
want
to check out. That would be to fix b1=1 in the model. In
toxicology
parlance, the simplified model would imply that you would be
fitting a
discrete Michaelis Menten model - with your modification to have
vary
the intercept with latency - rather than a modification of a Hill
model.
The Michaelis-Menten based model will have some linear slope at low
dose
(may be steep, but would not become "infinitely steep" as get close

to
zero dose). Of course you would have find out through trying
whether
the simpler model provided an adequate fit to the data.
The reason I suggest trying this is that my hunch is Bill's
bootstrap
analysis is giving very low BMDL is because some of the bootstrap
resamples have fits with Hill exponent (b1, that is) with values
less
than one. In that case, the Hill model can become extremely steep
at
the lowest doses (and infinitely steep as approach zero). Thus if
the
simpler Michaelis-Menten model works for the data set, it would
seem
that it may more likely yield plausible BMDL values.
Just offering this for your consideration...
Paul